PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference JA920177	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2004/016761	International filing date *(day/month/year)* 11 November 2004 (11.11.2004)	Priority date *(day/month/year)* 14 November 2003 (14.11.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant HUMAN CELL SYSTEMS, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 27 July 2006 (27.07.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Masashi Honda e-mail: pt08@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference JA920177	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/016761	11.11.2004	14.11.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant
HUMAN CELL SYSTEMS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016761

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☒ in computer readable form

   c. time of filing/furnishing

      ☒ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016761

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	5-11	YES
	Claims	1-4	NO
Inventive step (IS)	Claims		YES
	Claims	1-11	NO
Industrial applicability (IA)	Claims	1-11	YES
	Claims		NO

2. Citations and explanations:

(Documents cited in the International Search Report)
Document 1: WO 2002/000210 A2 (Merck and Company Incorporated), 03 January 2002
Document 2: JP 2003-093067 A (Hitoshi ENDO), 02 April 2003
Document 3: Atsushi ENOMOTO et al., Molecular identification of a renal urate-anion exchanger that regulates blood urate levels, Nature, 23 May 2002, 417(6887), pp. 447-452
Document 4: Hirokazu YOKOYAMA et al., "Nyousan transporter to tokuhatsusei jinsei teinyousankesshou", 25 June 2003, Molecular Medicine, Vol. 40, No. 7, pp. 762-767
Document 5: Atsushi ENOMOTO et al., "Nyousan transporter to jinsei teinyousankesshou", Rinshou Byouri, 20 September 2003, Vol. 51, No. 9, pp. 892-897
Document 6: Hitoshi ENDO et al., Transporter to shikkan, Pharmacia, 01 May 2003, Vol. 39, No. 5, pp. 431-435

Claims 1-4

The inventions described in Claims 1-4 do not appear to be novel based on document 1 cited in the ISR.

Document 1 describes that administration of a drug that can lower urate levels, such as the probenecid or benzbromarone given as examples of "drugs having the effect of inihibiting the urate uptake effect of URAT1" in the specifications of this application, is useful in treating or preventing hypetension, cardiovascular disease and kidney disease caused by hyperuricemia.

Claims 1-11

The inventions described in Claims 1-11 do not appear to involve an inventive step over documents 1-6 cited in the ISR.

As described in documents 1-3, it is publicly known that hypertension, cardiovascular disease and renal disorder are caused by hyperuricemia, and that drugs capable of lowering uric acid levels are useful in the treatment and prevention of such diseases.

(Continued in Supplemental Box)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016761

Box No. VIII **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-4 relate to a drug composition for the therapy, prevention or treatment of vascular disorder, hypertension and renal disorder having as an active component a compound defined by the desired properties of "a drug having the effect of inhibiting the uric acid uptake effect of URAT1" and "a URAT1 inhibiter or blocker". Claims 1-4 encompass all compounds having these properties, but only a very small part of the claimed compounds is supported by the specifications in the sense of PCT Article 6 or disclosed in the sense of PCT Article 5.

Moreover, regarding "a drug having the effect of inhibiting the uric acid uptake effect of URAT1" and "a URAT1 inhibiter or blocker," the scope of compounds having such properties cannot be specified in light of technical common knowledge at the time of the application; therefore Claims 1-4 also do not fulfil the requirement of clarity under PCT Article 6.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

Moreover, document 2 describes a protein (urate transporter 1) having the ability to transport uric acid and uric acid analogues, along with a method of using that protein to screen substances having uric acid excretion regulation effects, and describes that the urate transporter URT1 has the ability to transport uric acids and uric acid analogues from one side of the cell membrane to the other, that it is a uric acid/anion exchanger which uses anions on the other side of the cell membrane as the exchange substrate, and that a novel compounds that the discovery of novel compounds that inhibit the function of this transporter and control factors that modulate its expression would contribute to the development of new treatment methods for hyperuricemia and gout.

Moreover, documents 3-6 describe that the urate transporter URAT1 is involved in uric acid uptake into cells, that uric acid transport by URAT1 is inhibited by probenecid, benzbromarone and other hyperuricemia treatment drugs, that that this molecule is involved in the mechanism by which these drugs promote uric acid excretion, and they describe that URAT1 is an intermediary for drugs that alter uric acid levels and a drug creation target for new drugs that promote uric acid excretion..

Thus, it would be easy for a person skilled in the art to use a drug having the effect of inhibiting the uric acid uptake effect of URAT1 or a URAT1 suppressor or blocker in the therapy, prevention or treatment of vascular disorder, hypetension or renal disorder caused by hyperuricemia, thereby achieving the inventions of Claims 1-4.

Moreover, specific screening methods, etc. for effective substances are commonly selected as appropriate according to the objective by those skilled in the art in the field of drug preparation, and it would be easy for a person skilled in the art to use a cell system expressing URAT1 to screen effective substances for the therapy, prevention or treatment of vascular disorder, hypertension or renal disorder caused by hyperuricemia and to select the measurement conditions as appropriate, thereby achieving the inventions of Claims 5-11.